

Dear Professor Ivanovics:

Thank you for your letter of August 21, which I received a few weeks ago, and am answering at my first opportunity.

First, I wonder if you are raising your questions with a competent authority. The question of terminology of S-R variation is primarily one of immunology, not of genetics. However, it seems to me that S-R variation has acquired a more or less generally accepted meaning as pertaining to loss of a protein-carbohydrate complex, the "somatic antigen" which, in many species is associated with pathogenicity. More loosely, it has been applied to the loss of any major antigenic constituent—e.g. the capsular polysaccharide of the pneumococcus.

In my own opinion, this terminology is based on an incorrect interpretation of the antigenic structure of different bacteria, and is therefore so inexact to begin with that there is no point in arguing about its application. The distribution, and relative importance in immunology and infection, of different components is very different from one bacterial species to another, and there is simply no homology between the components of *B. megaterium*, say, and *Salmonella typhimurium*, to justify a uniform notation. In my opinion, therefore, "R-S" notation is purely colloquial, and has no precise meaning when applied to bacteria other than the enteric bacteria for which it was developed. For this reason, I myself would prefer to ~~disregard~~ disregard the R-S notation, in favor of a precise statement of the immunochemical alteration. I suspect my immunological colleagues will not all favor this proposal.

It is of some interest that your "rough" isolates were also nonmotile. Have you tried to select motile "reversions" from these cultures, for example by inoculation in semi-solid agar?

To make a more concrete proposal, I believe you could designate your mutants as  $Cp^b$  from  $Cp^a$  or some similar term, intended only to express a change in a capsular reaction. Am I correct in understanding that the variant produces the same poly-glutamic polypeptides as the wild type. [[[\* perhaps better  $Zw^a$  to  $Zw^b$ ]]].

In my use and understanding of the term "mutation" means any hereditary change in the quality of an organism, i.e., a change inherent in the organism and not simply a direct response to the environment. There is no question that your variation in the  $Zw$  character fits this definition of a mutation. It would require further analysis to define the locus of this mutation, whether it is in the "chromosomes" or whether it is autonomously determined by the  $Zw$  itself.

I am enclosing a note that may interest you. I understand your countrymen ~~Yakov~~ Vahasz and Horvath may have interests in common with mine, but I do not know where to contact them: can you furnish their addresses?

Yours sincerely,

Joshua Lederberg  
Professor of Genetics